REMARKS

Claims 31-35, 38, 39 and 63, and 65-70 are pending in the application.

Claims 31-35, 38, 39, 63 and 65-67 have been rejected under 35 U.S.C.§112, first paragraph as allegedly not enabled. Applicant respectfully traverses this rejection.

It is respectfully brought to the Examiner's attention that there have been numerous office actions (several phone calls to Applicant's representative prior to the first Office Action in which the Examiner requested certain claim amendments which when made were promptly rejected in the first office action, three more office actions and an advisory action) over the past four years and this is the first time that the Examiner has asserted that the claimed invention is not within the scope of the specification with respect to enablement of "alternative wash, elution buffers, sample sizes" as recited on pages 3-4 of the Office Action. Further, Applicant made every claim amendment suggested by the Examiner in the interview of June 25, 2002 to address section 112 rejections. The Examiner appeared satisfied in the last office action of September 11, 2002 that there was no more section 112 issues. Now the Examiner has decided to make this new section 112 rejection that could have been made in the first office action. Applicants contend that the Examiner is not being fair to Applicant in that there appears to never have made a thorough examination in the first place. This statement is being made for the record because the Applicant intends to appeal this application if this continues further and has already notified the Examiner's supervisor.

With respect to the new section 112, first paragraph rejection, Applicants assert that one of ordinary skill in the art would easily know which wash buffer, elution buffer, sample size and reaction conditions would be suitable for the purification of RNA and DNA according to the invention. It is submitted that the purification of RNA and DNA, as it has been described in the specification and claims, relates to lysing cells to free the nuclear content thereof so that the nuclear content can be removed from the reservoir tube with the wand provided. The method of the invention is described at page 10, lines 12-20, page 7, last paragraph through page 9 line 24. The broad concept and practice of the

removal and separation of RNA and DNA from cells is not new. Applicants presented to the Examiner a copy of a paper by Boom, et al., incorporated by reference at pages 8-9 of the specification for its teaching of "The capture of nucleic acids, proteins or cells either non-specifically or by affinity binding onto solid supports" (spec., page 8, first paragraph). Applicants provided the pages of Boom, et al that clearly identified the subject matter which is incorporated by reference (pages 495-503 of Boom et al. as indicated at page 9, line 15). Boom et al. makes clear that one of ordinary skill in the art at the time of the invention would be able to determine the type of wash buffer, type of elution buffer, amount of sample and conditions necessary to practice the invention. Boom et al. does not, however, disclose the reservoir tube or the wand of the present invention. It is the technique of using a reservoir tube and wand in the method of the invention that is asserted to be novel. Further, the Applicants even provided an example to show how to practice the method of the claims using the reservoir tube and wand.

The Examiner's new assertion that the subject incorporated by reference is improper is without merit. The first sentence of the first full paragraph on page 8 of the specification recites:

The capture of nucleic acids, proteins or cells either non-specifically or by affinity binding onto solid phase supports as well as colorimetric, luminiscent, fluorescent and electrochemical detection are well known in the art as described in the following and other references, of which these are incorporated by reference:

This statement clearly indicates why the numerous publications are incorporated by reference, i.e. to show how to capture nucleic acids, proteins or cells..... Most of the references indicate the specific page numbers as well as volume numbers and dates so the requirement of showing where to find the incorporated subject matter has been met in the present specification.

Applicants respectfully submit that the claims are enabled by the specification and could be practiced by one of ordinary skill in the art based on the level of skill in the art as indicated by the references that have been incorporated by reference.

The Examiner also asserts that the RNA would be destroyed by the method of the present invention. The Applicant has performed many tests according to the claimed method and RNA is not destroyed. Further, one of ordinary skill in the art practicing the invention by the methods outlined in the specification and as claimed would not expect the RNA to be destroyed by ribonucleases as asserted by the Examiner. The procedures for purification of RNA and preserving its integrity are well known in the art. Voluminous articles in the literature teach the processes which deal with purification of nucleic acids from a variety of sample types. A list of the articles which deal with such processes were submitted in the disclosure. Usually a strong denaturant is used in the initial step to disrupt the cells and release nucleic acids. Examples of strong denaturant include guanidinium isothiocyanate (GITC), LiCl, SDS and phenol. These denaturants render RNases inactive. The use of GITC was mentioned in the body of the invention disclosure, and the use of other denaturants was cited by reference (See Current Protocols in Molecular Biology. Greene Publishing Associates and Wiley-Intersciences. John Wiley & Sons, New York, Chichester, Brisbane, Toronto, Singapore; Sambrook J., Fritsch EF, Maniatis J. (1989). Molecular cloning: A laboratory manual. 2nd edition, Cold Spring Harbor laboratory Press, Cold Spring Harbor, New York.). In the present invention, after applying the appropriate protocol to release RNA from a given sample, non-specific capturing of RNA onto the capture assembly, the captured RNA can be washed several times with RNAse-free washing buffer, then the RNA is eluted from the capture assembly by using an elution buffer. The Lysis/binding, washing and elution buffer conditions may be adapted according to the sample type and the type of the nucleic

acids (DNA or RNA). If the isolated RNA is to be stored for later use, it is critical that the RNA is kept in a Rnase-free solutions that contains a chelating agent, such as Sodium Citrate (1 mM, pH 6.4); EDTA (0.1 mM) in DEPC-treated ultrapure water, or TE buffer (10 mM Tris-HCl, 1 mM EDTA pH 7) and kept at –20oC. For long-term storage, RNA can be kept -80°C. Any individual skilled in the art can practice the invention to isolate high quality RNA by applying the basic guidelines for working with RNA. Such guidelines as frequently changing gloves, using RNase-free tips, tubes, and solutions and decontaminating pipettors and benchtops are well known and routinely practiced by researchers who deal with RNA work.

It is respectfully submitted that the present claims are in compliance with section 112, first paragraph and this rejection is overcome.

Claims 31-35, 38, 39, 63 and 65-70 are rejected under 35 U.S.S. 103(a) as being unpatentable over Van Ness et al. in view of Boom et all., JP 7-308184A and Wiggins. Applicant respectfully traverses this rejection.

Applicant's last amendment only corrected the dependency of claims 68 and 69. No other amendment to the claims was made that would have necessitated grounds for a new search. Applicant wonder why these new references were never cited in the previous Office Action dated September 11, 2002 or at any other times over the past four years. Again, Applicants assert that they were never given a thorough examination in the first place and have had to endure great expense as a result.

The present claims under examination are directed to a purification method for recovering purified DNA or RNA from a sample using an assembly as claimed that requires a wand having a cap, a shaft and a sample collection assembly with microstructures. The claims also call for reservoir tubes that are securely and sealingly closed by the cap on the wand. The purpose for this unique design is at least two fold and solves two problems at once. First the microstructures are present to increase the surface

area of the sample collection assembly to capture a greater amount of nucleic acids. Secondly, the use of the wand and reservoir tubes permits a military service member or other user to perform nucleic acid purification of a sample out in the field, for example during a military action where there is no electricity to vortex a sample. A user can simply agitate the reservoir tubes with the wand/sample collection assembly in place to cause the desired reaction to occur.

Bringing the answer to these two problems into a single apparatus and method has not been disclosed or suggested by any of the cited references.

Van Ness et al. is directed to compositions and methods for covalently immobilizing an oligonucleotide onto a polymer coated bead or similar structure. Van Ness et al. does not disclose or suggest the use of a wand and reservoir tube to collect nucleic acids where the reservoir tube is sealingly secured to the cap of the wand as required by the present claims. A user of the method of the present invention can use reservoir tube and wand assembly in the field by simply agitating the assembly by hand because of the claimed "seal" of the cap to the reservoir tube.

A dipstick is suggested by Van Ness that comprises a nonporous solid support having a means for attaching beads. The dipstick disclosed in Van Ness et al. is non-porous. The sample collection assembly in the present claims has microstructures. Further, as stated by the Examiner, Van Ness et al. also does not disclose the binding of nucleic acids to a silica oxide support and elution and purification of the captured nucleic acids. Van Ness et al. is only concerned with immobilization of oligonucleotides and not purification. Van Ness et al. also does not disclose a need for microstructures or for sealingly closing the cap to the reservoir tube. Therefore, Van Ness et al. is different in scope and purpose and does not lead one of ordinary skill in the art to the present invention.

Boom, et al. is directed to a method for the purification of nucleic acids. Boom et al. discloses the use of silica particles to capture nucleic acids. However, the silica particles are free floating in solution and are not attached to a "sample collection assembly" on a wand. Further, Boom et al. does not suggest any need to attach the silica particles to a "sample collection assembly" on a wand. Thus, Boom et al. does not

render obvious the presently claimed invention that requires "*said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly.*" Boom et al. does not solve the problems that the present invention is designed to solve as stated above. Therefore, Boom et al. does not add anything to Van Ness et al. to lead one of ordinary skill in the art to the present invention.

JP-7-308184 shows a tube and a wand. The Examiner asserts that a seal is formed between a cap and the tube. Applicants request the Examiner to point out where in this reference it is stated that a seal is formed. No translation of the abstract has been provided to Applicants. The Examiner asserts that the wand can be used for the collection of biological samples that are later used for PCR. However, there is no suggestion of performing the method of the present invention with such steps as agitating the reservoir tube to mix the sample under conditions for releasing DNA or RNA. Further, there is no suggestion of using multiple reservoir tubes or of using microstructures on the wand. Therefore, JP7-308184 does not suggest the claimed method of the invention or provide any motivation for modifying Van Ness et al. or Boom et al.

Wiggins is directed to compositions and methods for isolating nucleic acids from biological tissues and cells and for tissue/cell solubilization for other molecular biological. The method in Wiggins uses gravity or centrifugation and not agitation as claimed in the present invention. There is also no disclosure of the use of multiple reservoir tubes, a wand or a sealing engagement of a cap to a reservoir tube. Wiggins only discloses eluting captured nucleic acids from a solid support such as co-polymer beads. Therefore, Wiggins does not make up for the deficiencies of the other references which fail to disclose the use of multiple reservoir tubes, sealed caps, wands with microstructures and the purification of DNA and RNA with such a device.

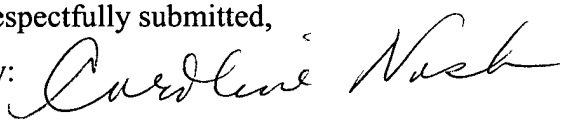
In conclusion, none of the cited references, whether taken alone or in combination, would have lead one of ordinary skill in the art to the present invention because none of them provide a method for DNA or RNA purification that employs a

wand having a sample collection assembly with microstructures. No single invention or combination of inventions cited by the Examiner contains all the features claimed in the present invention in terms of simplicity and adaptability. Further, none of the references provide the required motivation in the form of a single statement or suggestion to make their combination as required by 35 U.S.C. §103(a) that would have lead one of ordinary skill in the art to the presently claimed invention. The mere assertion that that several references could have been combined without any supporting phrase by even one comment in any of the references that supports their combination is insufficient to uphold this rejection. Therefore, the rejection under 35 U.S.C. §103(a) is believed overcome.

Reconsideration and allowance are respectfully requested. The Examiner is invited to telephone Applicant's representative at (301) 924-9500 if it would in any way expedite prosecution.

Respectfully submitted,

Date: June 25, 2003

By: 

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